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3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

GlaxoSmithKline Biologicals s.a.
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Patents ADP number *(if you know it)*

Belgian

If the applicant is a corporate body, give the country/state of its incorporation — 81012710 01

4. Title of the invention — Process

5. Name of your agent *(if you have one)*

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Process

This invention relates to a novel process for manufacturing medicinal vials. Medicinal vials are widely used for containing pharmaceutical product to be dispensed by injection. Pharmaceutical products include drugs and vaccines in a solid (e.g. lyophilised) or liquid (e.g. solution) state, for either prevention and treatment of human and animal diseases and conditions, or diluent and reconstitution materials etc. Such vials usually comprise a vial body made of glass, or of a medically acceptable polymer such as cycloelefin copolymers ("COC"), blends thereof or blends thereof with other polymers. Examples of such polymers are for example disclosed in US-A-5723189, EP-A-0436372 and EP-A-0556034 among others. A suitable hard plastic material accepted for use in the pharmaceutical industry is the cyclolefin copolymer "Topas" made by Celanese Corporation. The vial body normally has a mouth opening which is closed by a puncturable closure, generally made of an elastomer, many of which are known. Normally the pharmaceutical product content is extracted from the vial in a well known manner by passing a hollow injection needle through the puncturable closure. It is known to injection mould and assemble Topas syringes in a robotic clean room (www.plasticstechnology.com).

A process is known from for example EP-A-0678574 and WO-A-02/064439 in which an empty vial closed with a puncturable closure is provided, pharmaceutical product content is introduced into the vial via a hollow needle passed through the closure, the needle is withdrawn from the vial and closure, and the residual puncture hole is sealed by heating the closure material around the puncture site for example with a laser beam. The closure part may for example be made of a blend of the polymers "Engage" supplied by Dupont-Dow, and "Dynaflex" formerly known as "Kraton" as supplied by Shell but now available from GLS (USA) who supply this blend, and including a dye, e.g. grey, to enhance absorption of laser light so that the elastomer material may be heated using laser light. With this process it is important for the interior of the vial body and at least the part of the closure in contact with the interior of the vial body to be in a sterile condition before the pharmaceutical product content is introduced. For use in this process empty vials with their closure in place may be sterilised by radiation

directed at the vials and passing through the vial and closure material, but this radiation sterilising procedure introduces cost and complexity because of the need for a radiation source. Vials, closures and a vial-closure combination suitable for such a process are disclosed in GB patent application GB 0219152.6 filed 16 August 2002 by the same applicant as this application, the contents of which are incorporated herein by reference. WO-A-02/064439 discloses vial closures suitable for such a process having a lower infusible portion and a thermoplastic upper part which can be heat sealed e.g. with a focussed laser.

It is an object of the present invention to provide a process by which a medicinal vial having its mouth closed by a puncturable closure and with its interior in a sterile condition may be made, suitable for use in the above described process. Other objects and advantages of the process of the invention will be apparent from the following disclosure.

According to this invention a process for making a medicinal vial comprises:

(1) providing a mould having an openable cavity therein defining the shape of a medicinal vial having a mouth opening,

(2) moulding a vial in the mould cavity using a mouldable medicinally acceptable polymer,

(3) opening the mould to expose the so-formed vial,

(4) removing the so-formed vial body from the mould,

(5) automatically inserting a sterile puncturable closure into the mouth opening of the so-formed vial body using automatic mechanical handling means,

and wherein at least steps (3) to (5) are performed under sterile conditions.

A preferred embodiment of the process of the invention comprises:

(1) providing a mould having an openable cavity therein defining the shape of a medicinal vial having a mouth opening,

(2) moulding a vial in the mould cavity using a mouldable medicinally acceptable polymer,

(3) opening the mould to expose the so-formed vial,

(4) removing the so-formed vial from the mould,

(6) providing a mould having an openable cavity therein defining the shape of a puncturable closure for the mouth opening of the medicinal vial,

(7) moulding a puncturable closure in the mould cavity using a mouldable medicinally acceptable elastomeric polymer,

(8) opening the mould to expose the so-formed puncturable closure,

(9) removing the so-formed puncturable closure from the mould,

(5) automatically inserting the so-formed puncturable closure into the mouth opening of the so-formed vial,

and wherein at least steps (3), (4), (5), (8) and (9) are performed under sterile conditions.

The invention also provides an apparatus for performing the above-described process. Such an apparatus may comprise:

(A) a first mould having an openable cavity therein defining the shape of a medicinal vial having a mouth opening, and in which a vial may be moulded using a mouldable medicinally acceptable polymer, and which may be opened to expose a vial moulded therein,

(B) a second mould having an openable cavity therein defining the shape of a closure for a medicinal vial when moulded in the first mould, and in which a closure may be moulded using a mouldable medicinally acceptable polymer, and which may be opened to expose a closure moulded therein,

(C) automatic mechanical handling means adapted to insert a puncturable closure made in the second mould into the mouth opening of a vial made in the first mould,

(D) means to provide a sterile environment in relation to (A), (B) and (C) such that said first and second moulds may be opened, a respective vial and closure may be removed from the respective first and second moulds, and the closure inserted into a vial, in the sterile environment.

The process and apparatus of this invention addresses the above-mentioned problem by enabling the vial and a closure to be made by respective moulding processes from respective suitable polymers, such as those mentioned above, and then immediately or as soon as practical after manufacture the closure to be inserted into the mouth of the vial under conditions which minimise the possibility of contamination of the vial and closure. In the process of the invention the vial is made and subsequently closed by the closure in a sterile environment without being

transferred to a storage area between moulding and sealing, so there is no or very little opportunity for contamination of the vial before sealing.

In typical moulding processes the polymer, conventionally supplied in a pellet form, is subjected to a high temperature to melt the polymer and is forced by high pressure into the mould, and the temperature and pressure conditions typically employed are generally sufficient to destroy any micro-organisms that might be contaminating the polymer and thereby sterilise the polymer.

The mould(s) for use in the process of the invention, i.e. the first and second moulds of the apparatus, may a blow mould in which the vial or closure is moulded by gas pressure from a so called pre-form. Alternatively and preferably the mould may be an injection mould in which solid polymer is fluidised by heat and pressure typically by a helical screw, and is then forced under pressure into the mould cavity. Such an injection mould may be a so called hot or cold runner mould, preferably a hot runner mould. The mould may be single or preferably multi cavity.

The shape of the so-formed vial and consequently the mould cavity should be designed so that the mould can be opened easily, i.e. without "overhangs". A suitable shape for the vial is an internally and preferably externally cylindrical tubular shape, with an open end defining a mouth opening, and an opposite closed end, with a flange externally around the mouth opening. An internally cylindrical shape enables the cylindrical interior of the vial to be defined by a corresponding cylindrical core of the mould and from which the vial can be smoothly withdrawn to separate the so-formed vial from the mould. Externally the closed end of the vial may be formed with an engagement part for the automatic mechanical handling means, described in more detail following.

The closures may comprise a single elastomer, or alternatively they may be of the type disclosed in WO-A-02/064439 having a lower infusible portion and a thermoplastic upper part which can be heat sealed, and the mould may be configured to make closures of this type.

The moulding processes and general construction and operation of the moulds for making the vial and closure may be generally conventional, and it is preferred that the moulding equipment used is of a pharmaceutically acceptable GMP standard.

Suitable polymers for the vial are the above mentioned polymers. Using a COC or COC -based polymer cycle times of ca. 10-15 seconds can be achieved in the manufacture of a typical 2.5 – 100 ml capacity vial. For example the known COC polymer Topas 8007 may be used, available from for example Ticona GmbH (DE). Conditions for injection moulding this polymer are known in the art. Topas 8007 has a glass transition temperature of ca. 85°C if used it is preferred that the formed vial is ejected from the mould before it has cooled to below ca. 70°C. An alternative COC polymer is Topas 6015, and if this polymer is used it is preferred that the formed vial is ejected from the mould before it has cooled to below ca. 110-120°C. It is preferred not to use any mould release agent.

It is found that the cycle time for moulding of the elastomeric closures may be longer than that of the polymeric vials because the closures take longer to cool and harden because of among others their greater wall thickness, softness and lower thermal conductivity. Typically a cycle time of 15-20 seconds may be achieved.

When the vial is of the above mentioned cylindrical shape with a cylindrical interior the mould is preferably constructed such that when the mould is opened in step (3) the vial is retained, prior to ejection, on the mould by means of a cylindrical core part of the mould extending into the cylindrical interior defined by the core, and so that the so-formed vial may be ejected and removed in step (4) from the mould by sliding the vial off the core part along the length axis direction of the cylinder. The mould(s) provided in steps (1) or (6) for making the vial and closure suitably comprise an ejector means, which may be generally conventional, to eject the so formed vial or closure from the respective mould.

The automatic insertion of the closure into the mouth opening of the vial in step (5) may be done using automatic mechanical handling means, preferably being done as soon as practical after the vial and closure have been ejected from the mould and if necessary after performing any re-orientation of the vial and/or closure to facilitate the insertion. Such means may comprise a robot configured to receive and releasably engage with the formed vial or closure during or after ejection from the mould and to remove the same from the vicinity of the mould, although the automatic handling means may itself be configured to remove the formed vial or closure from the mould. For example the automatic handling machinery may

comprise a robot arm moveable between a first position proximate to the mould and a second position distanced from the mould, the arm having vial or closure engaging means.

Preferably such a robot, e.g. by means of its arm, engages with the exterior of the closed end of the vial, i.e. being distant from the mouth opening to reduce the possibility of contamination of the interior of the vial.

Preferably such a robot, e.g. by means of its arm, engages with a part of the closure which will not be in contact with the interior of the vial when the closure is in place to thereby reduce the possibility of contamination of surfaces exposed to the interior of the vial.

Suitable means by which the robot may releasably engage with the vial or closure will be apparent to those skilled in the art, for example gripping jaws. However it is preferred that the vial or closure engaging means comprises a vacuum suction means, i.e. that draws the vial or closure into contact with the engaging means. A vacuum suction means complies with GMP and avoids complex mechanisms such as pinching fingers, and is easy to clean and maintain. To facilitate engagement of the robot arm with the vial the exterior of the closed end of the vial may include a part with which the robot may engage. Analogous machinery may be used with the closure. Suitable robot machines are known or conventional, and it is preferred that such machines as used are of a pharmaceutically acceptable GMP standard. Robots provided by Stäubli AG (CH) are considered to be suitable, being available in a form qualified to work in Class 10 on silicon wafers in the electronics industry.

In the preferred embodiment of the process it is preferred that the process steps (7) – (9) in which a closure is made are performed in parallel with steps (2) – (4) in which the vial is made, so that the processes for making the vials and for making the closures are performed substantially simultaneously. In this way as soon as a vial has been made a closure is available to close it, and as soon as a closure has been made it is ready to be inserted into a vial. This facilitates the making of a vial and the making of a closure then immediately or very shortly after the vial and closure are in a suitable state to be engaged, e.g. when they have sufficiently hardened and/or cooled, inserting the closure into the vial mouth, and doing so

whilst the vial and closure are in the sterile environment. For example closures may be engaged with the vials within 10-20 seconds of the mould in which the vial is made being opened. Therefore the vial and closure can be made in a sterile state in the moulding operation, then engaged, all within a sterile environment.

As mentioned above the respective cycle times for moulding of vials and closures may be different, that of the closures generally being longer than that of the vials. To compensate for this the mould in which closures are made may comprise more, suitably twice the number, of cavities than the mould in which vials are made.

In the preferred form of the process and apparatus of the invention one handling means holding or otherwise engaged with a closure can introduce the closure into a vial whilst the vial is held or otherwise engaged by another handling means. One of the handling means may release the vial or the closure so that the engaged vial and closure may be retained by the other, preferably by the handling means which initially handled the vial. For this purpose the respective vial and closure moulding and automatic handling machinery may be positioned adjacent each other so that e.g. one handling robot can offer the closure to the vial being handled by another handling robot.

After the vial and closure have been assembled, i.e. the closure has been inserted into the mouth of the vial, the assembly of vial and closure may be transferred automatically, e.g. by automatic handling machinery, to a further processing station at which further processes may be performed on the assembly, preferably automatically and preferably also within the sterile environment.

A preferred further processing step is that of securing the closure to the vial using a clamp means, by engaging a suitable clamp means with the assembly of vial and closure. Conventionally closures are secured in place on the mouth of a vial by means of a clamp means that urges the closure against the rim of the vial mouth opening or against a flange surrounding the mouth opening. Such clamps may be made of metal, but it is preferred to use a clamp part made of plastics material, which may be engaged with the vial and closure by snap fitting, e.g. by a relative downward movement of the clamp part relative to the combination of vial and

closure. The engaging of such a clamp part may be done whilst the combination of vial and closure are still in the sterile environment.

For example as disclosed in above-mentioned GB patent application GB 0219152.6 filed 16 August 2002 a clamp part may be engaged with the vial, particularly with the rim of the mouth opening, and able to bear upon the upper surface of the closure part to hold the closure part in a closing relationship with the mouth opening. Such a clamp part may, as disclosed in above-mentioned GB 0219152.6 have an aperture therein through which a region of the upper surface of the closure part is exposed when the clamp part is engaged with the vial. A cover part as disclosed in above-mentioned GB 0219152.6 may be engaged with the clamp part and/or the vial to cover the said region of the closure part, a lower surface of the cover part facing the upper surface of the closure part when so engaged. As disclosed in GB 0219152.6 the cover part may have a sealing ridge projecting therefrom to a sealing edge that follows a closed perimeter, so that when the cover part is engaged with the clamp part and/or the vial the sealing edge engages with the closure part to form an enclosure with the closure part, at least that part of the cover part which includes the sealing ridge being removable from engagement with the clamp part and/or the vial.

This further processing may also be performed using automatic machinery, for example comprising a conveyor to transfer the assembly of vial and closure away from the point at which the closure is inserted into the vial mouth..

Steps (3) – (5) and in the preferred form steps (3) – (5) and (8) and (9) are performed under sterile conditions, i.e. within the sterile environment of the apparatus. By "sterile" is meant complying with accepted standards in the pharmaceutical or vaccine industry for the filling of vials with medicinal contents for subsequent injection into a human patient. Generally sterile conditions are defined in terms of a classification e.g. Class 100 being more sterile, 10,000 being less sterile etc., but the term "sterile" as used herein refers to any acceptable standard of environmental purity as required by local standards. Such sterility may be achieved by the use of standard sterilisation techniques and operation in a purified air environment.

For example the respective moulds may open, and the vial and closure may be assembled, within a sterile environment provided by a downward laminar air flow, typically class 100. (However the respective polymers for the vial and stopper may by fed into the respective moulding machines from outside of such an environment, the moulding conditions being suitable to sterilise the polymers). The automatic handling machinery of step (5) may operate entirely within the environment of this laminar airflow. When the vial and closure have been assembled so that the sterile integrity of the interior is maintained, the assembly may be transferred to a processing station for further processing as described above which is also in a sterile environment, but which may be of a lower degree of sterility to that in which the mould is opened and the vial and closure assembly assembled, for example class 10,000.

To maintain sterile conditions the mould and automatic handling machinery may for example be constructed and configured so that at all times during the procedure no part of the vial or closure is ever downstream in the sterile laminar airflow of any part of a mould or of the automatic handling machinery or any other equipment, so as to reduce the possibility of contamination being swept from the mould, machinery or other equipment onto the vial or closure. For example with a downward laminar flow the mould(s) may be configured to open in steps (3) and (8) along a horizontal axis, the automatic handling machinery may be configured to move a closure and vial together horizontally in step (5).

It may be unnecessary for the entire injection moulding machine, e.g. its polymer feed system, compression screw(s), heater etc. to be within a sterile environment, and this machinery may be located outside of the sterile environment, for example only the moulds and immediately adjacent parts of the machinery being within the sterile environment.

The invention also provides a combination of vial and closure when made by such a process.

Although the process disclosed herein is described in general terms it will be appreciated that all variations within this generally are encompassed within the scope of the present invention.

The process and apparatus of the invention will now be described by way of non-limiting example only with reference to the accompanying drawings.

Fig. 1 shows a vial and closure in longitudinal section, assembled and unassembled.

Fig. 2 shows an injection mould for making a vial

Fig. 3 shows the mould of Fig. 2 opened.

Fig. 4 shows an injection mould for making a closure

Fig. 5 shows the mould of Fig. 4 opened.

Fig. 6 shows the layout of a facility for performing the process.

Fig. 7 shows the arrangement of mould cavities.

Fig. 8 shows a vacuum gripping means for a vial.

Fig. 9 shows a vacuum gripping means for a closure.

Fig. 10 shows a clamp means fitted to a combination of vial and closure.

Parts referred to in Figs 1-10 and the related description are identified below.

10 vial

11 open end

12 mouth opening

13 flange

14 closed end

15 profiled outer bottom surface

20 elastomeric closure

21 lower plug part

22 flange

23 upper dome-shaped puncturable part

30 part of an injection mould

31,32 two mould blocks

33 cavity

34 split line

35 injection port

36 core

37 surface

40 injection mould

41,42 mould blocks

43 cavity

45 injection port

46 core

47 surface

50 sterile area

51 walls of sterile area

52,53 injection moulding machines

54 sub-area

55,56 automatic handling machinery

57, 58 robot arm

59, 510 vacuum handling

511 vacuum port

512, 513 airlocks

60 further processing station to fit clamp parts

61 clamp part

62 snap fit teeth

63 snap fit groove

70 conveyor

Referring to Fig. 1 a vial 10 and elastomeric closure 20 are shown in longitudinal section in both an unassembled and assembled configuration. For clarity the clearance between the closure 20 and vial 10 is shown exaggerated. The vial 10 is externally and internally of cylindrical tubular shape with an open end 11 defining a mouth opening 12 which is surrounded by a flange 13. The vial 10 has an opposite closed end 14, with a concave profiled outer bottom surface 15 comprising an engagement part for the automatic mechanical handling means, described in more detail following. The vial 10 is made of a COC polymer.

The closure 20 comprises a lower plug part 21 shaped and dimensioned to fit conformingly and tightly into mouth opening 12 of the vial 10, a flange 22 shaped and dimensioned to fit conformingly and tightly against flange 13, and an upper dome-shaped puncturable part 23. The closure 20 fits in place into the vial mouth

12 as shown in Fig. 1, and as secured by the clamp part 61 later described forms a tight micro-organism proof seal.

Fig. 2 shows part of an injection mould 30 in which the vial 10 may be made. The mould 30 comprises two mould blocks 31, 32 between then defining a cavity 33 which is openable by splitting the mould at split line 34 and which defines the shape of the vial 10. There is an injection port 35 via which a fluid polymer such as COC or a COC-based polymer may be injected under appropriate temperature and pressure conditions known in the art for injection moulding of such polymers.

The mould 30 is a hot runner multi cavity mould typically comprising plural cavities 33. It is seen that the above-described shape of vial ensures that there are no "overhangs" obstructing removal of the formed vial 10 from the mould. Fig. 3 shows how when the vial 10 has been made in the mould 30 the mould 30 may be split at line 34, leaving the formed vial 10 retained upon the part 36 of the block 31 that comprises a core defining the cylindrical shape of the interior of the vial 10.

Fig. 4 shows part of an injection mould 40 in which the closure 20 may be made. The mould 40 comprises two mould blocks 41, 42 between then defining a cavity 43 which is openable by splitting the mould at split line 44 and which defines the shape of the vial 20. There is an injection port 45 via which a fluid elastomeric polymer may be injected under appropriate temperature and pressure conditions known in the art for such materials. The mould 40 is a hot runner multi cavity mould typically comprising plural cavities 43. It is seen that the above-described shape of closure 20 ensures that there are no "overhangs" obstructing removal of the formed vial 20 from the mould. Fig. 5 shows how when the closure 20 has been made in the mould 40 the mould may be split at line 44, leaving the formed closure 20 retained upon the part 46 of the block 41 that comprises a core defining the domed internal shape of the closure 20.

Moulds 30 and 40 also include conventional ejection machinery (not shown) to eject the formed vial 10 and closure 20 from the moulds 30, 40.

The moulds 30 and 40 are set up and operated as shown schematically in plan in Fig. 6. A sterile area 50 maintained dynamically at class 10,000 is provided within the walls 51 of a clean room. Generally conventional injection moulding

machines 52, 53 for respectively feeding the moulds 30, 40 for making the vials 10 and closure 20 are provided. These machines 52, 53 are hot runner machines and conventionally comprise a reservoir of polymer material (not shown) and a conventional screw extruder with conventional heating equipment etc. (not shown). These machines are constructed to pass through the wall 51 so that they can be driven, maintained and fed with polymer feed from outside of the area 50, with a sterile seal between the wall 51 and machines 52, 53. Each machine 52, 53 is constructed so that its respective mould 30, 40 opens in the manner described above within the area 50, and within a sub-area 54 which is maintained at class 100 by means of a downward sterile laminar airflow.

Each mould 30, 40 is set up so that it opens and closes horizontally at the respective line 34, 44, i.e. opening along an axis perpendicular to the surface 37, 47, such that the surface 37, 47 of each mould when open is in a vertical plane parallel to the sterile laminar airflow to reduce the possibility of any part of the mould 30, 40 being upstream in the laminar flow of air in area 54. Using a COC polymer in mould 30 and conventional injection moulding conditions a cycle time of ca. 10-15 seconds can be achieved in the manufacture of a typical 2.5 – 100 ml capacity vial 10. In the process of the invention both moulds 30 and 40 are operated in parallel, i.e. vials 10 and closures 20 are made simultaneously. The cycle time for making closures 20 is longer than the cycle time to make vials 10 because the relatively thick walled closures 20 take longer to cool. Consequently as shown in Fig. 7 the mould 40 in which the closures 20 are made comprises twice as many cavities 43, i.e. sixty-four cavities 43 arranged in four rows each of sixteen cavities 43 as does the mould 30 in which vials 10 are made, mould 30 comprising thirty-two cavities 33 arranged in two rows of sixteen cavities 33.

Within the area 50, and operating within sub-area 54, automatic handling machinery 55, 56 is provided. Each machine 55, 56 comprises a robot arm 57, 58 which is capable of being moved into a first position shown in dashed lines adjacent to a respective mould 30, 40 when the mould 30, 40 is open. Each robot arm 57, 58 has at its extremity one or more vacuum handling means 59, 510 as shown in Figs. 8 and 9 of a shape complementary to and able to engage by suction with a surface of respectively the vial 10 and closure 20 which when the vial and closure are

assembled as shown in Fig. 1 will not be in contact with the interior of vial 10. In the case of vial 10 this surface is the outer concave bottom 15 of the vial, and in the case of the closure 20 this surface is the outside of the dome 23. Each vacuum handling means 59, 510 includes a vacuum port 511 through which vacuum may be applied. As each arm 57, 58 is moved adjacent to the respective mould 30, 40 the arm 57, 58 contacts the said surface of the vial 10 or closure 20, the vacuum handling means 59, 510 engages the vial 10 or closure 20. The ejection machinery (not shown) associated with each mould may then be operated to thereby remove the formed vial and closure from the respective mould 30, 40.

Then the arm 57, 58 is moved away from the respective mould 30, 40 to thereby carry the formed vial 10 and closure 20 from the respective mould 30, 40.

Each robot arm 57, 58 then moves to a second position shown in full lines in Fig. 6 at which the respective vacuum handling means 59, 510 and the respective vial 10 and closure 20 are adjacent to each other such that the plug part 21 of the closure 20 is inserted into the mouth opening 11 of a vial 10. This insertion operation is performed within the sub-area 54. The handling means 510 which engages the formed closure 20 then releases the closure 20 so that the assembly of vial and closure 10, 20 is held by the handling means 59 which holds the vial 20. Using multi-cavity moulds 30, 40 as shown in Fig. 5, plural handling means 510 are used to remove thirty-two formed closures 30 from mould 40 and to insert them into thirty-two corresponding vials 10 formed in mould 30 as described above. As the respective closures 20 and vials 10 have corresponding arrangements in rows in respective moulds 30, 40 two alternate rows of closures 20 are removed from mould 40 as shown in Fig. 7 whilst maintaining the arrangement of the closures 20, and inserted into corresponding vials 10.

When all of the vials 20 have been removed from mould 30 the mould 30 is closed to re-form the arrangement shown in Fig. 2, a further thirty-two vials 10 are made by injection moulding, the mould 30 is opened, and the procedure of inserting closures 20 into these vials as described above is repeated using the remaining alternate rows of thirty-two closures 20 in mould 40. When all of the sixty-four closures 20 have been removed from mould 40 the mould 40 is closed to re-form

the arrangement shown in Fig. 4 and a further sixty-four closures are made as described above.

It will be understood that the sterile areas 50 and 54 enable the above process to be performed under sterile conditions, and to maintain sterile conditions in area 50 operator and material access to area 50 may be via airlocks 512, 513. By making both the vial 10 and closure 20 in these moulding processes the polymers used are subjected to a high temperature and high pressure which destroy any micro-organisms that might be contaminating the polymer. As the vial 10 is sealed with closure 20 immediately after manufacture, in a sterile environment 54 there is no or very little opportunity for contamination of the vial before sealing.

After the vial 10 and closure 20 have been assembled as described above, the assembly of vial 10 and closure 20 may be transferred to a further processing station 60 comprising automatic handling machinery at which a clamp part (not shown), e.g. as described in GB patent application GB 0219152.6 onto the assembly to hold the closure 20 in place may be fitted onto the assembly of vial 10 and closure 20. Fig. 10 shows a combination of a vial 10 with a closure 20 in its mouth opening, with a clamp part 61 of the type disclosed in GB 0219152.6. The clamp part 61 comprises a resilient plastics material generally ring-shaped member, having snap fit engagement teeth 62 configured to snap resiliently underneath the flange 13 around mouth opening 12 of the vial 10 when moved relatively downwardly over the flange 13, and to hold the upper part of the clamp part firmly downwards against the closure 20. To do this the vial and closure combination 10,20 may be re-oriented by the handling machinery 60 into a vertical orientation. Clamp part 61 also includes a groove 63 by which a cover part (not shown) of the type disclosed in GB 0219152.6 may be engaged with the clamp means 61. The further processing station is shown within the sub-area 54 but may be outside, e.g. in the area 50 as the vial 10 is now closed by the closure 20.

After the clamp part 61 has been engaged with the combination of vial 10 and closure 20, these may be transferred by further automatic handling machinery 70 being a conveyor system by means of which the vials are transferred away from the robots 55, 56 for any further processing.

Automatic handling machinery 55, 56, 60, 70 etc. may be generally conventional and suitable machinery will be apparent to those skilled in the art. Although shown as swinging robot arms 55, 56 other types and motions of robot arm may be used, such as X-Y-Z axis pick and place robots. Further handling machinery 60 may for example comprise a conveyor system to transport assembled vials 10 and closures 20 in the direction of the arrow. In the construction and arrangement of the moulds 30, 40 and the robot arms 55, 56 it is important that that at no time does any part of the mould 30, 40 or arms 55, 56 become upstream of the vial or closure made or handled thereby, to avoid any possibility of contamination of vial-closure assemblies by particles carried by the laminar airflow from the mould 30, 40 or arm 55, 56 toward the respective vial or closure. For example as shown in Fig. 7 the cavities 43 in which closures are made may be staggered in adjacent rows.

Claims.

1. A process for making a medicinal vial comprising:

(1) providing a mould having an openable cavity therein defining the shape of a medicinal vial having a mouth opening,

(2) moulding a vial in the mould cavity using a mouldable medicinally acceptable polymer,

(3) opening the mould to expose the so-formed vial,

(4) removing the so-formed vial body from the mould,

(5) automatically inserting a sterile puncturable closure into the mouth opening of the so-formed vial body using automatic mechanical handling means,

and wherein at least steps (3) to (5) are performed under sterile conditions.

2. A process according to claim 1 comprising:

(1) providing a mould having an openable cavity therein defining the shape of a medicinal vial having a mouth opening,

(2) moulding a vial in the mould cavity using a mouldable medicinally acceptable polymer,

(3) opening the mould to expose the so-formed vial,

(4) removing the so-formed vial from the mould,

(6) providing a mould having an openable cavity therein defining the shape of a puncturable closure for the mouth opening of the medicinal vial,

(7) moulding a puncturable closure in the mould cavity using a mouldable medicinally acceptable elastomeric polymer,

(8) opening the mould to expose the so-formed puncturable closure,

(9) removing the so-formed puncturable closure from the mould,

(5) automatically inserting the so-formed puncturable closure into the mouth opening of the so-formed vial,

and wherein at least steps (3), (4), (5), (8) and (9) are performed under sterile conditions.

3. An apparatus for performing a process according to claim 1 or 2 comprising:

(A) a first mould having an openable cavity therein defining the shape of a medicinal vial having a mouth opening, and in which a vial may be moulded using a mouldable medicinally acceptable polymer, and which may be opened to expose a vial moulded therein,

(B) a second mould having an openable cavity therein defining the shape of a closure for a medicinal vial when moulded in the first mould, and in which a closure may be moulded using a mouldable medicinally acceptable polymer, and which may be opened to expose a closure moulded therein,

(C) automatic mechanical handling means adapted to insert a puncturable closure made in the second mould into the mouth opening of a vial made in the first mould,

(D) means to provide a sterile environment in relation to (A), (B) and (C) such that said first and second moulds may be opened, a respective vial and closure may be removed from the respective first and second moulds, and the closure inserted into a vial, in the sterile environment.

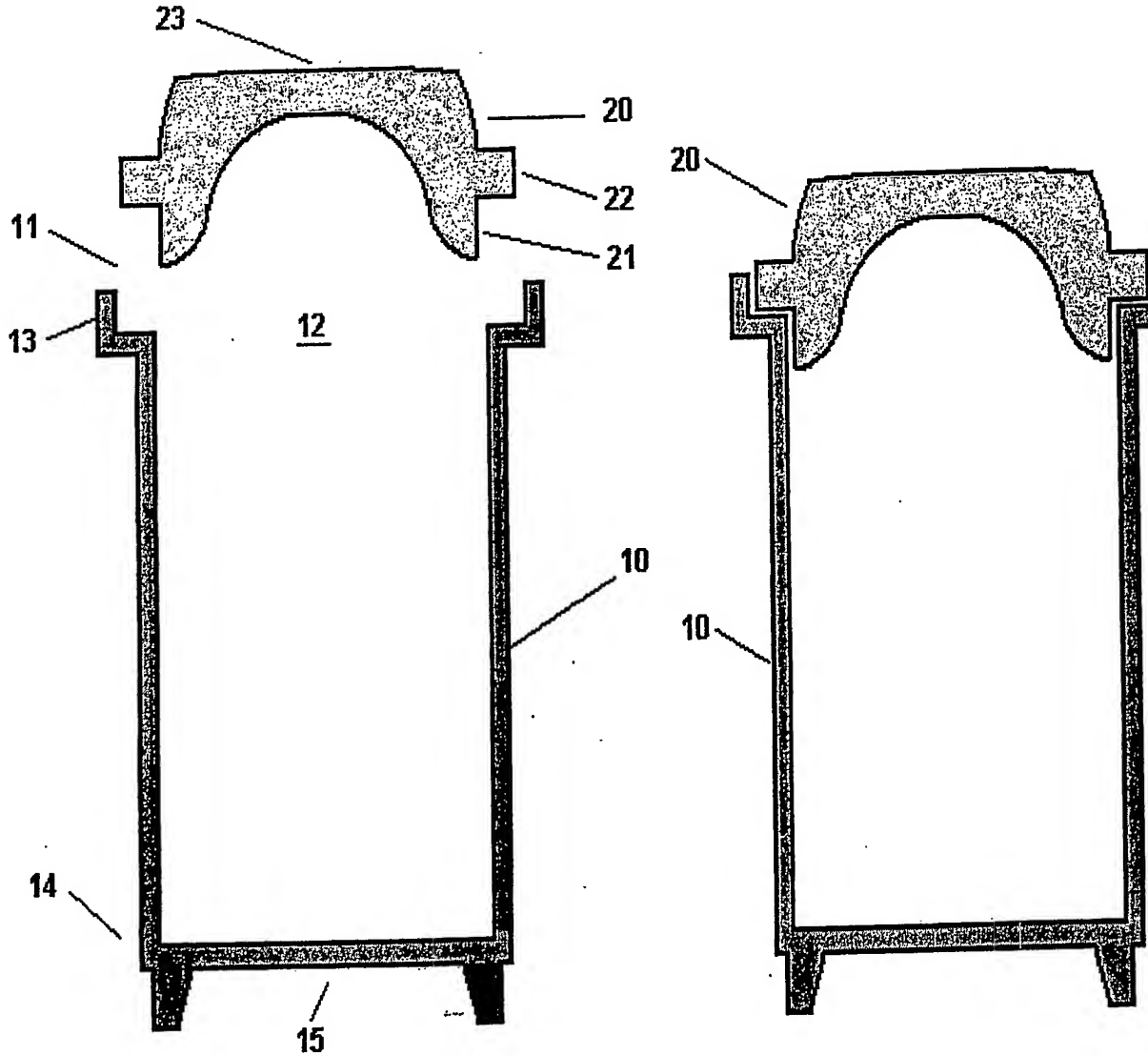

FIG. 1

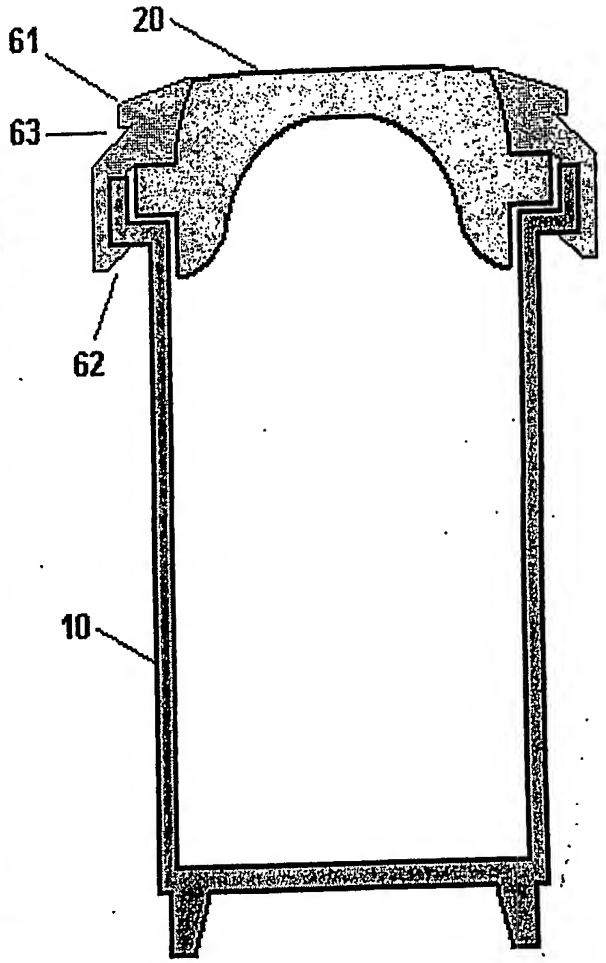

FIG. 10

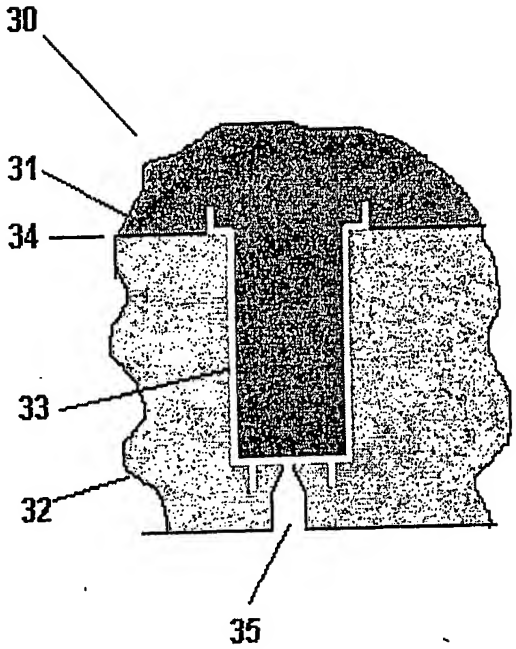

FIG. 2

FIG. 3

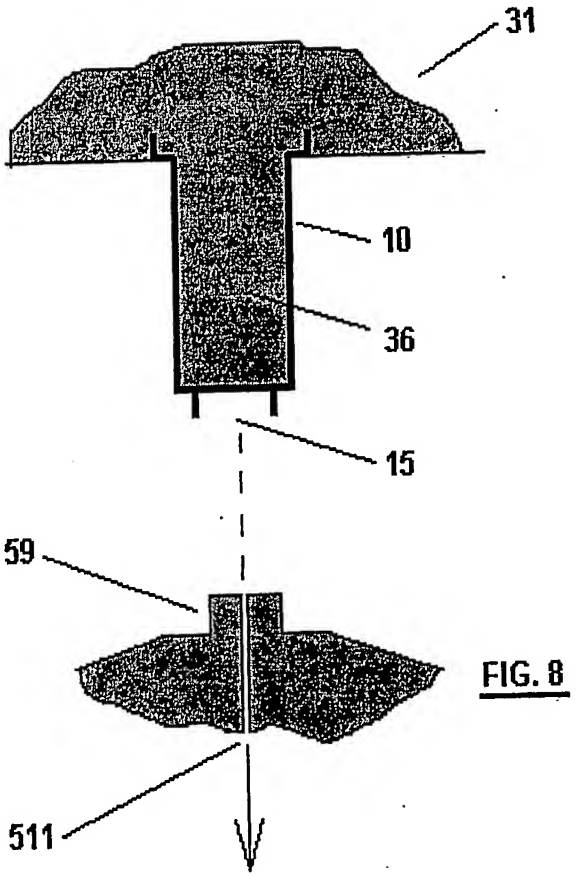

FIG. 8

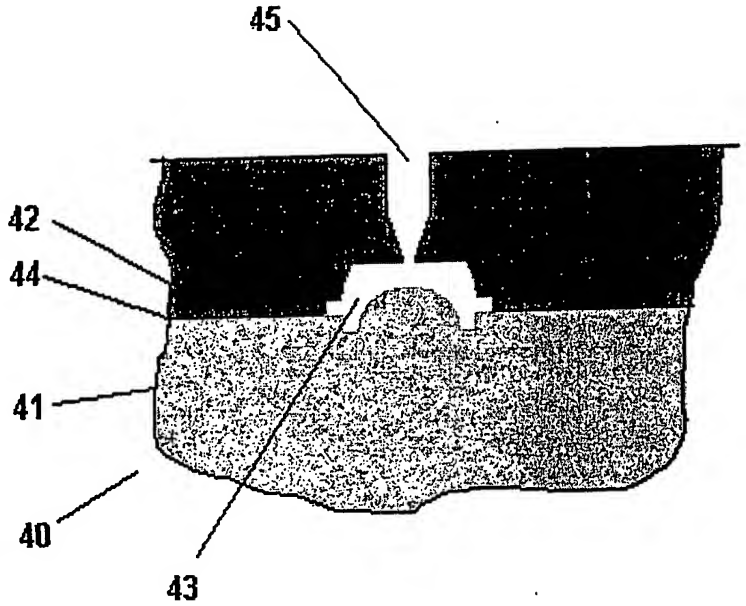

FIG. 4

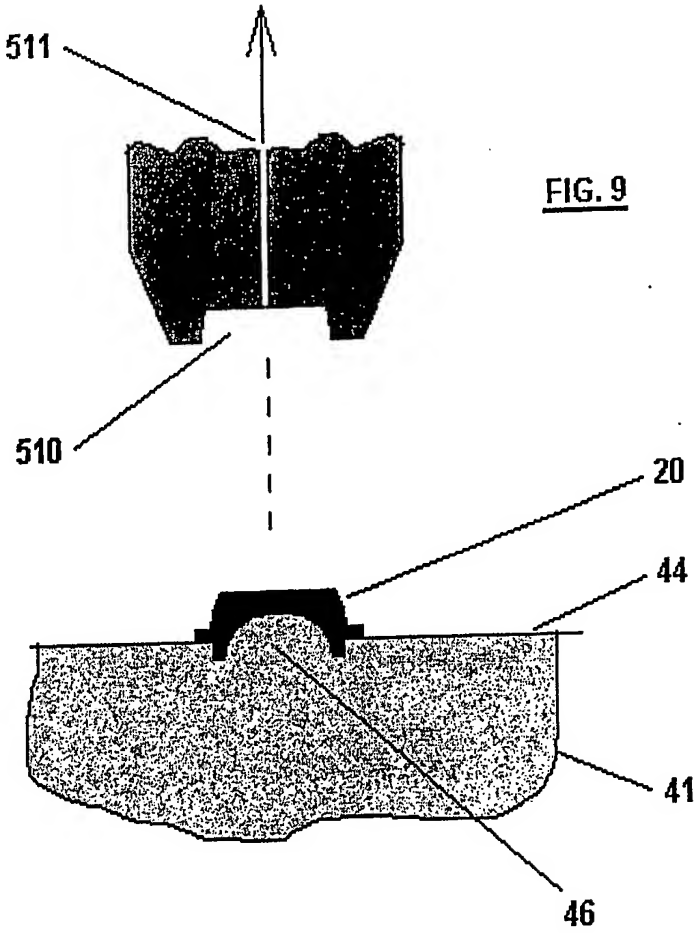

FIG. 5

FIG. 9

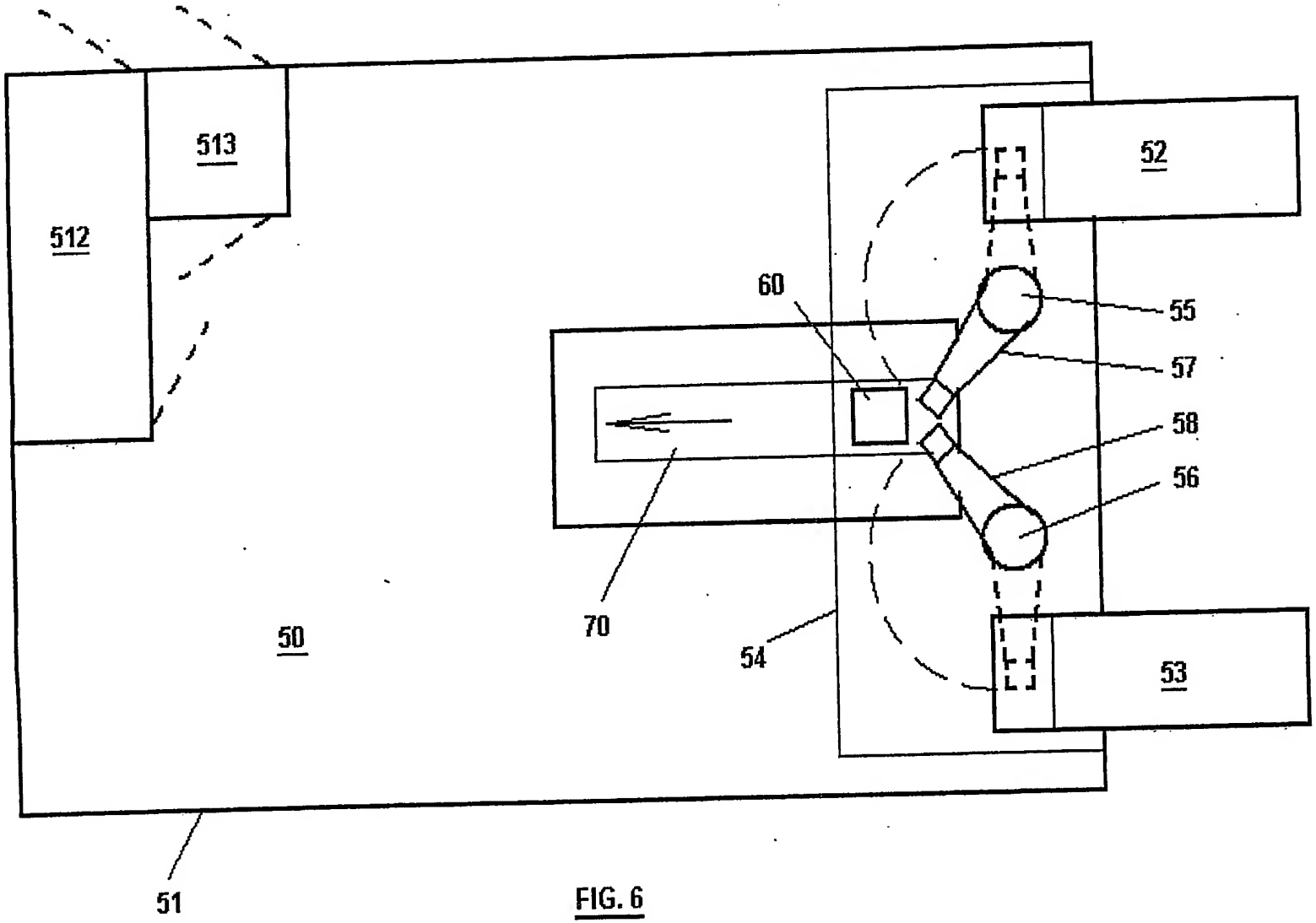

FIG. 6

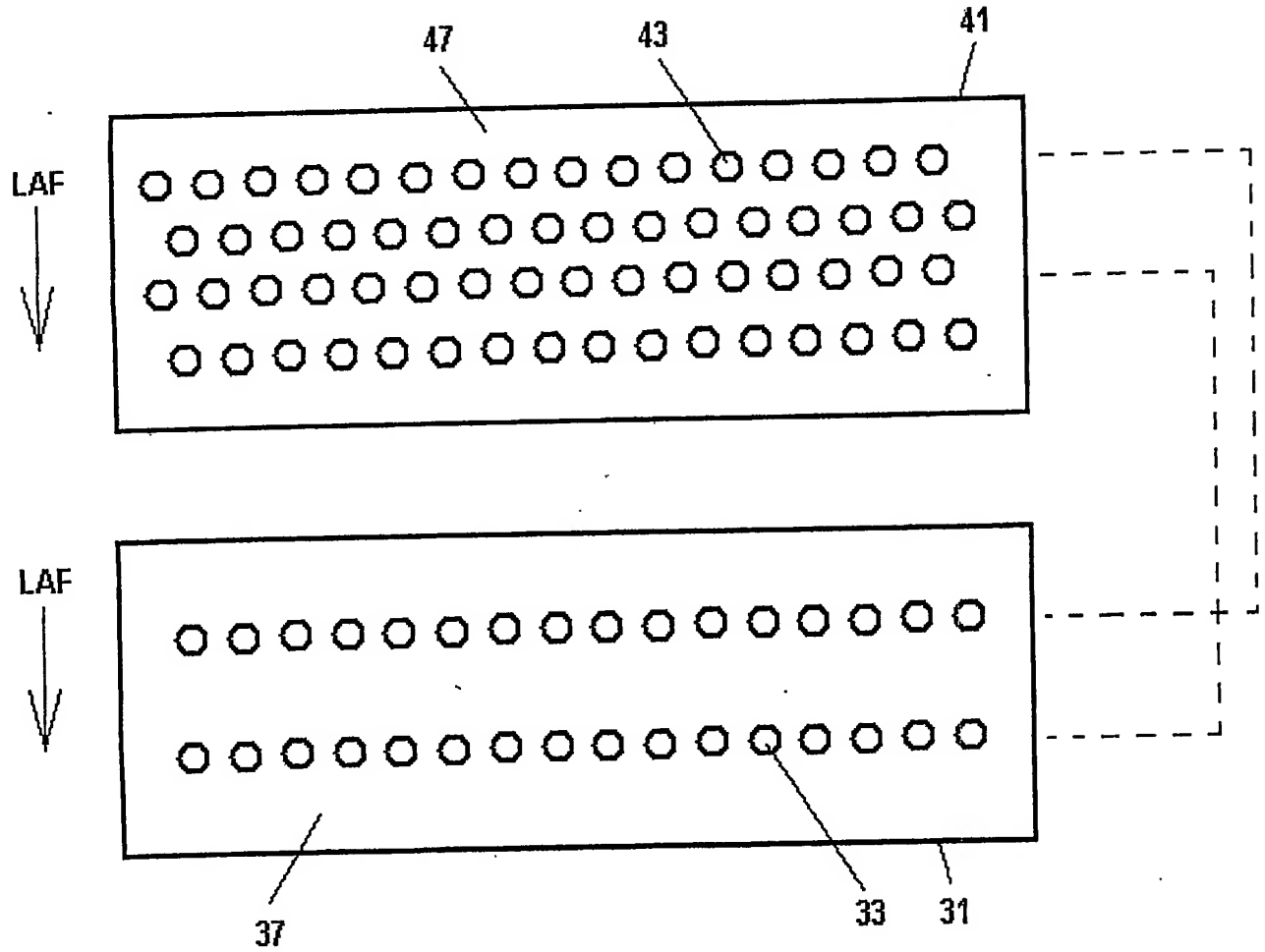

FIG. 7